Lessons learnt from reviewing SBE in the WHO African region

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World Health Organization

WHO global roadmap for snakebite

Goal: To half snakebite deaths by 2030

Four pillars:

- Empower and engage communities
- Ensure, safe effective antivenoms
- **Strengthen health systems**
- **Increase partnerships, coordination and resources**

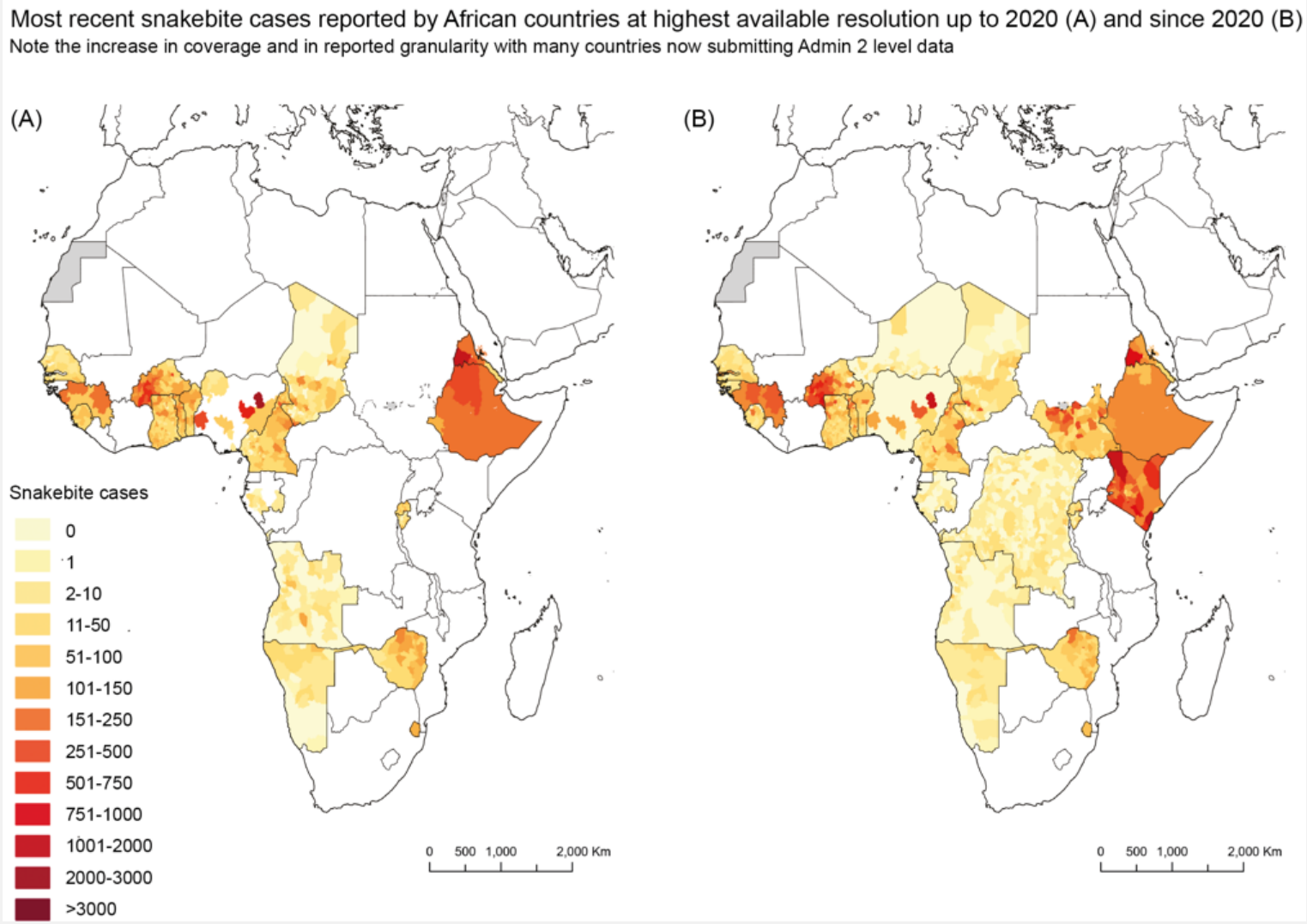
Better engagement by WHO with Member States improves epidemiology

Epidemiology data collection standardised in DHIS2/RHIS and GNARF

Core objective was to make it as easy as possible for people to report

Left – data before 2020

Right - data since 2020



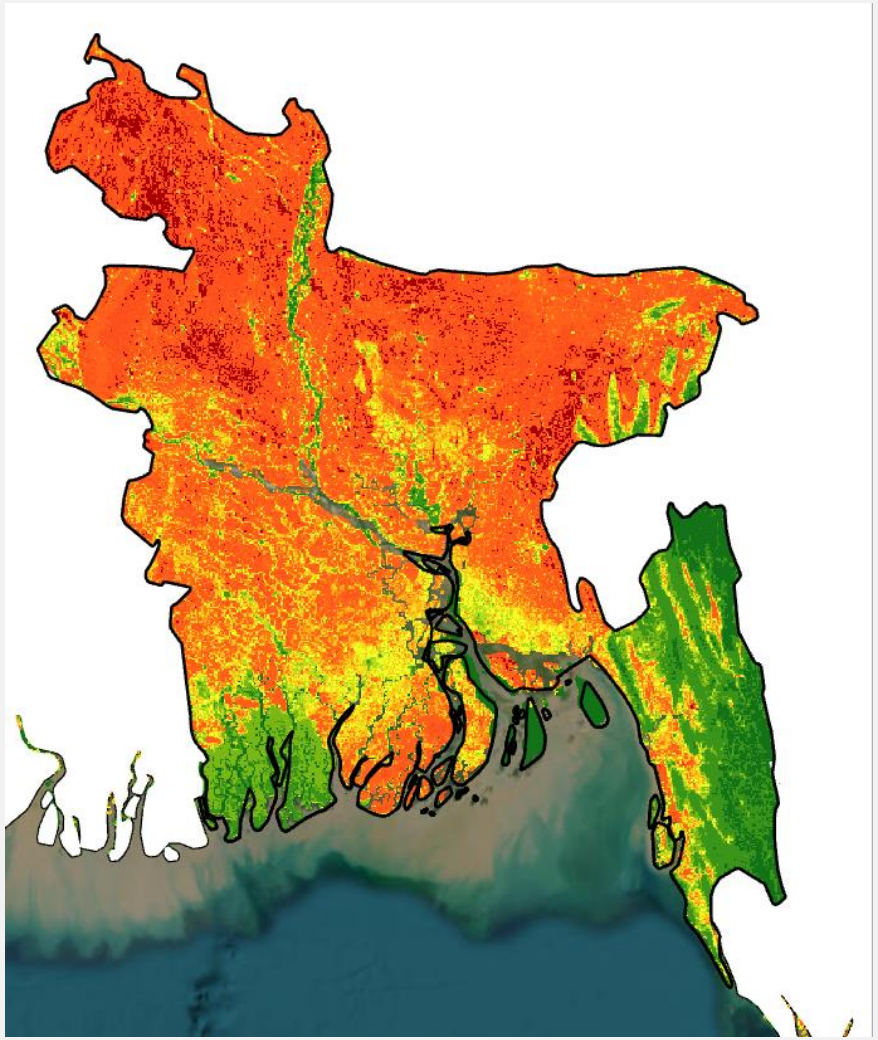
Epidemiological distribution studies can deliver more

2 weeks ago, Anna Pintor showed:

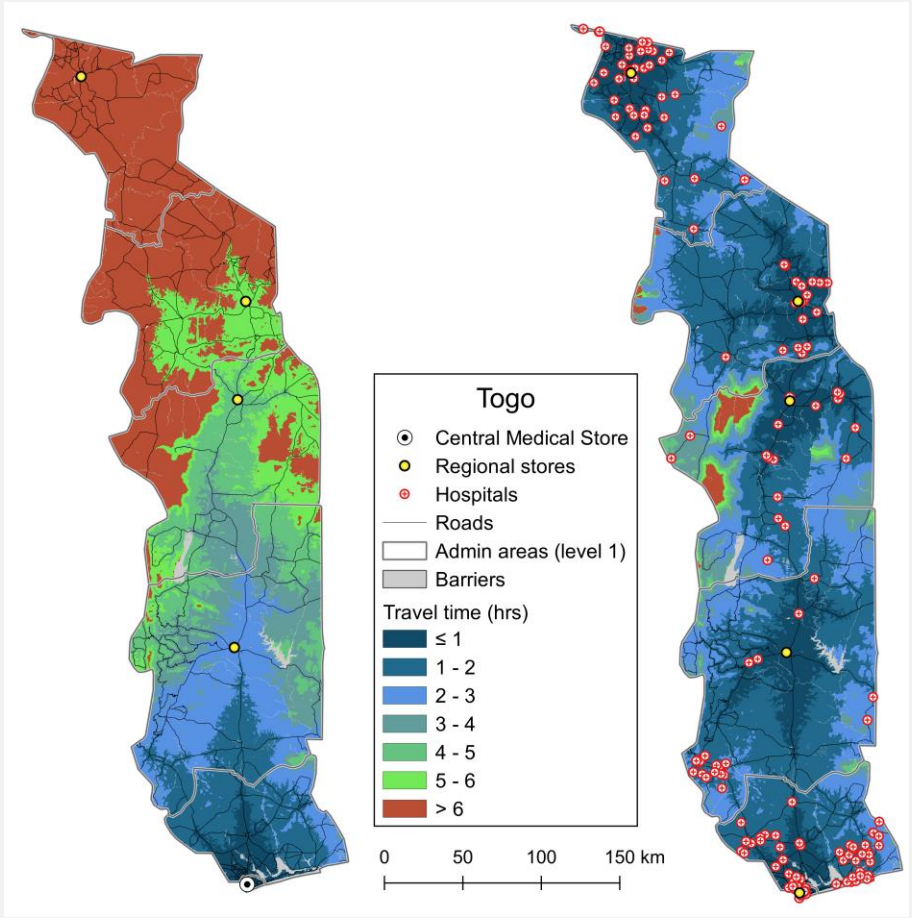
- Updated snake distribution maps
- Snake distribution modelling
- Snake- human regions of overlap

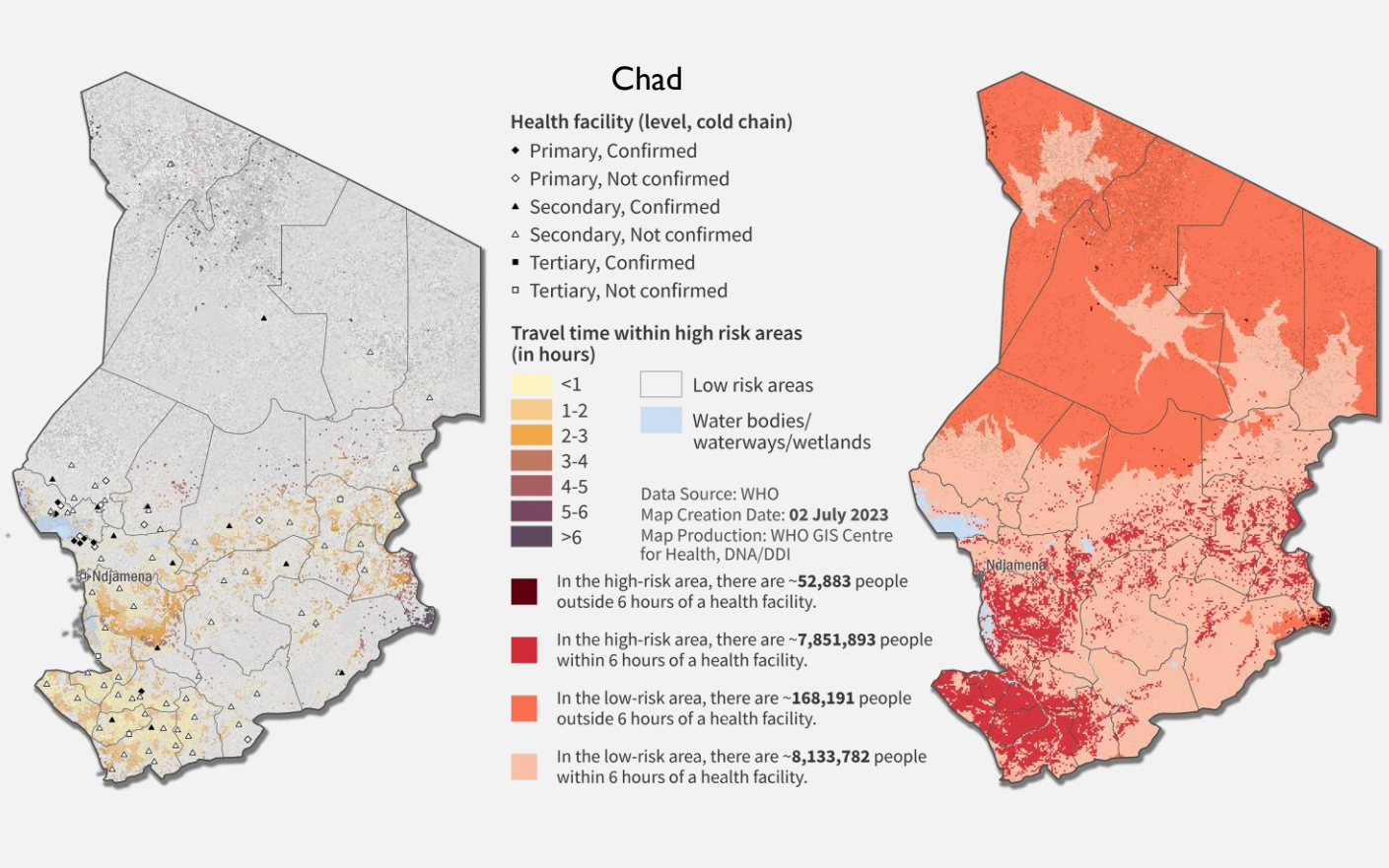
    To quantify where risk of snakebite is greatest

- But modelling can go further …….



Two examples of further mapping
(i) antivenom supply chain and distribution and
(ii) patient travel times





Antivenom Distribution Travel Times

Patient Travel Time to HC

Populations at Risk

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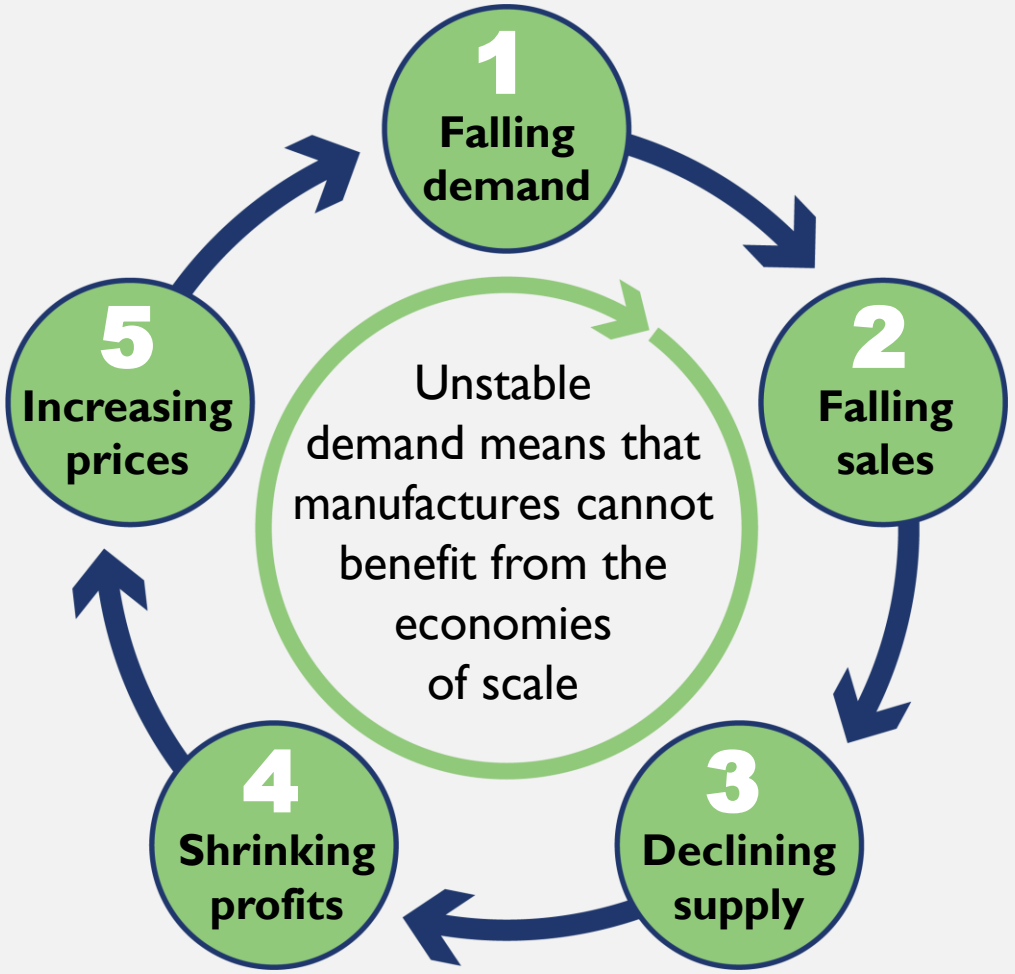
The antivenom market is failing



Widespread acceptance that antivenoms are of ‘variable’ quality

No guidance exists as to what would make them better/adequate

Target Product Profiles (TPPs) provide such guidance

What is a TPP?

- Ubiquitously used in industry for development of **new** pharmaceutical, medical, diagnostic products

- Also potentially useful to improve **existing** products

- It …. ‘outlines the desired ‘profile’ or characteristics of a target product that is aimed at a particular disease or diseases. TPPs state intended use, target populations and other desired attributes of products, including safety and efficacy-related characteristics’ [WHO]

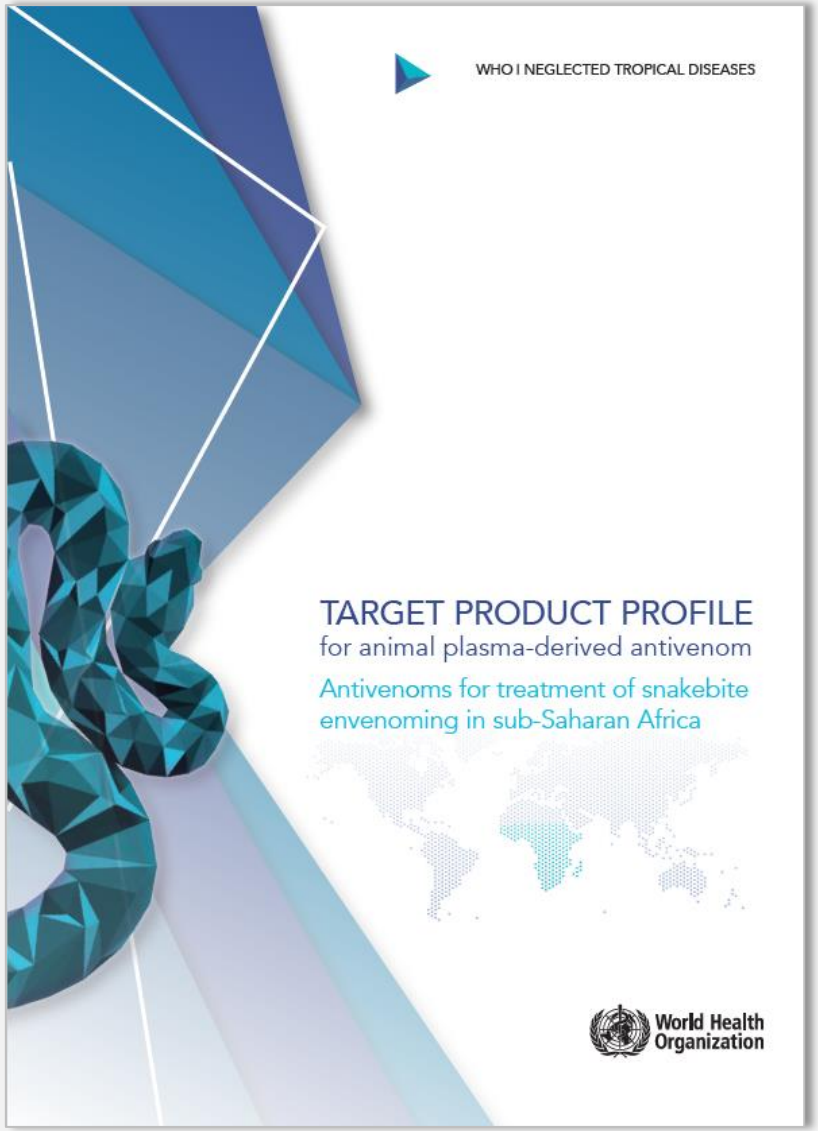
What does a TPP cover?

Areas covered	Examples
Scope	Target populations, geographic working ranges, indications for use, contraindications, level of implementation in health systems, intended end users
Manufacturing Considerations	Immunizing venoms, active pharmaceutical ingredient (API), finished product form, specific immunoglobulin content, total protein content
Performance	Preclinical efficacy, clinical effectiveness, safety and tolerability, drug interactions, dose regimen, frequency of administration, route of administration, product stability, storage, presentation, packaging
Operational Characteristics	Costs, supportive and adjunctive therapy, training and education needs

Target product profiles for antivenoms and other treatments

- Public-benefit TPPs have been developed for conventional animal plasma-derived antivenoms
- In development for small molecule and engineered antibody therapeutics
- Aimed at providing guidance to researchers, manufacturers, regulators and other stakeholders.
- Developed using standard WHO TPP methodology by a Technical and Scientific Advisory Group (TSAG) comprising a broad range of expertise
- Drafts are published on WHO website for public comment prior to finalization.
- Final documents published on website as PDFs for download:

https://www.who.int/teams/control-of-neglected-tropical-diseases/snakebite-envenoming/target-product-profiles



Selected line items from SSA antivenom TPP

Characteristic	Optimal	Minimal
Clinical effectiveness Polyvalent, monovalent and non-neurotoxic envenoming	When administered within 6-8 hours of a bite: • case fatality rate (CFR) to <1% • amputations to <1%. • persistence of coagulopathy at 24 hours post-antivenom to <3%. • debridement of dead tissue and/or skin grafting (not inc. blisters) to <5%.	When administered within 4-6 hours of a bite: • case fatality rate (CFR) to <2% • amputations to <2%. • persistence of coagulopathy at 24 hours post-antivenom to <6%. • debridement of dead tissue and/or skin grafting (not inc. blisters) to <10%.
Clinical effectiveness - neurotoxic envenoming	When administered within 6-8 hours of a bite: • case fatality rate (CFR) to <1% • debridement of dead tissue and/or skin grafting (not inc. blisters) to <5%.	When administered within 4-6 hours of a bite: • case fatality rate (CFR) to <2% • debridement of dead tissue and/or skin grafting (not inc. blisters) to <10%.

Staggeringly few clinical trials completed
'Optimal' is aspirational, but reasonable
'Minimal' is based largely on observational reports

Risk-benefit assessment progress for sub-Saharan African antivenoms

ASSESSMENT COMPLETED	ASSESSMENT IN PROGRESS	ASSESSMENT TERMINATED
• EchiTAbG™ *MicroPharm Limited* • Antivipmyn Africa® *Laboratorios Silanes, S.A. de C.V.* • PANAF™ Premium *Premium Serums & Vaccines*	• EchiTAb-plus-ICP *Instituto Clodomiro Picado* • BeAfrique-10 (Pan African), Be Afrique-6 (central Africa), and BeAfrique-1 (*Echis ocellatus*) *Biological E Limited* • SAIMR Polyvalent Antivenom *South African Venom Producers* • Snake Venom Antiserum (Afriven) I.H.S. (Lyophilised)*, Snake Venom Antiserum (*Echis*), Boomsven, and Afriven-S VINS Bioproducts Limited	• Inoserp™ PAN-AFRICA *Inosan Biopharma S.A.*

Our aim, by end of 2025, is risk-benefit assessed antivenoms in WHO catalog

World Health Organization | Prequalification of Medical Products
IVDs, Medicines, Vaccines and Immunization Devices, Vector Control

Contact us | Glossary and Acronyms | FAQ | Complaints

Product Streams | Events | News | eCTD | ePQS | About

V Vaccines

- About Vaccines Prequalification
- What We Do
- Documents A-Z
- List of Prequalified Vaccines
  - Prequalified vaccines
- Vaccines Eligible for WHO Prequalification
- Prequalification Procedures & Fees
- Post-prequalification Procedures
- Guidance Documents
- Prequalification Reports
- Emergency Use Listing Procedure
- Market Information
- Risk Assessment - Snake Antivenom
- eCTD

Prequalified Vaccines

Displaying: 1 - 3 of 3

Download list as CSV file

Vaccine type: Rabies | Commercial Name | Responsible NRA: - Any - | Manufacturer: - Any - | Pharmaceutical Form: - Any -

Number of Doses | Route of Administration: - Any - | Preservative: - Any - | Presentation: - Any - | Diluent: - Any -

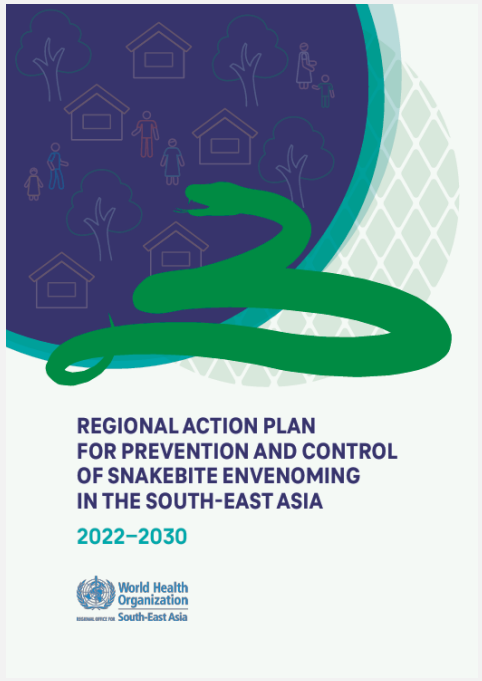
Shelf Life | Vaccine Vial Monitor: - Any - | Apply

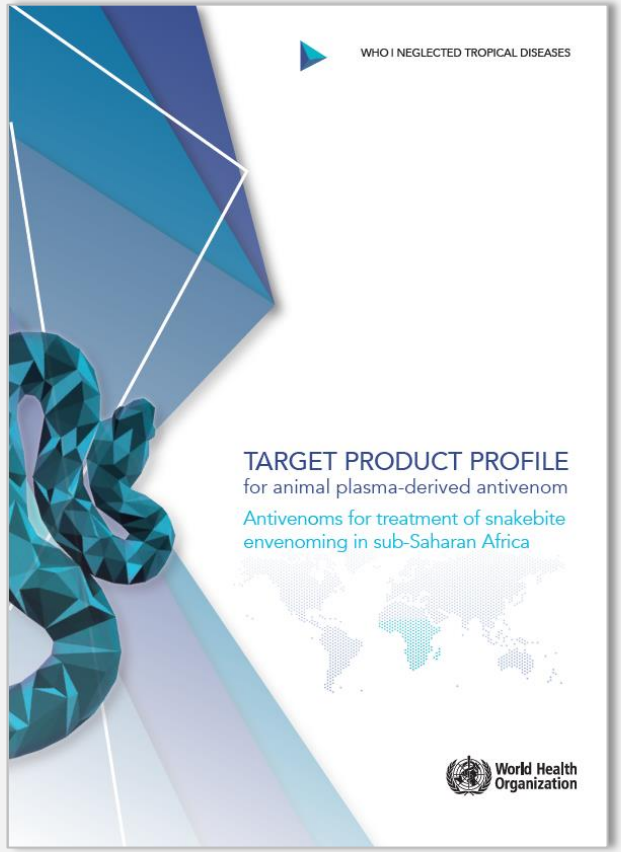
Date of Prequalification	Vaccine Type	Commercial Name	Presentation	No. of doses	Manufacturer	Responsible NRA
20/12/2018	Rabies	Rabies Vaccine Inactivated (Freeze Dried)(RABIVAX-S)	Vial + Ampoule	1	Serum Institute of India Pvt. Ltd.	Central Drugs Standard Control Organization
06/02/2019	Rabies	VaxiRab N	Vial	1	Zydus Lifesciences Limited	Central Drugs Standard Control Organization
22/06/2005	Rabies	VERORAB	Vial	1	Sanofi Winthrop Industrie	Agence nationale de sécurité du médicament et des produits de santé

CSV

Outputs and Outcomes - WHO

- Regional action plan SEARO
- Two new Target Product Profiles (third on the way) for antivenoms in sub-Saharan Africa and South Asia
- Catalogue listing of approved antivenoms (in process)



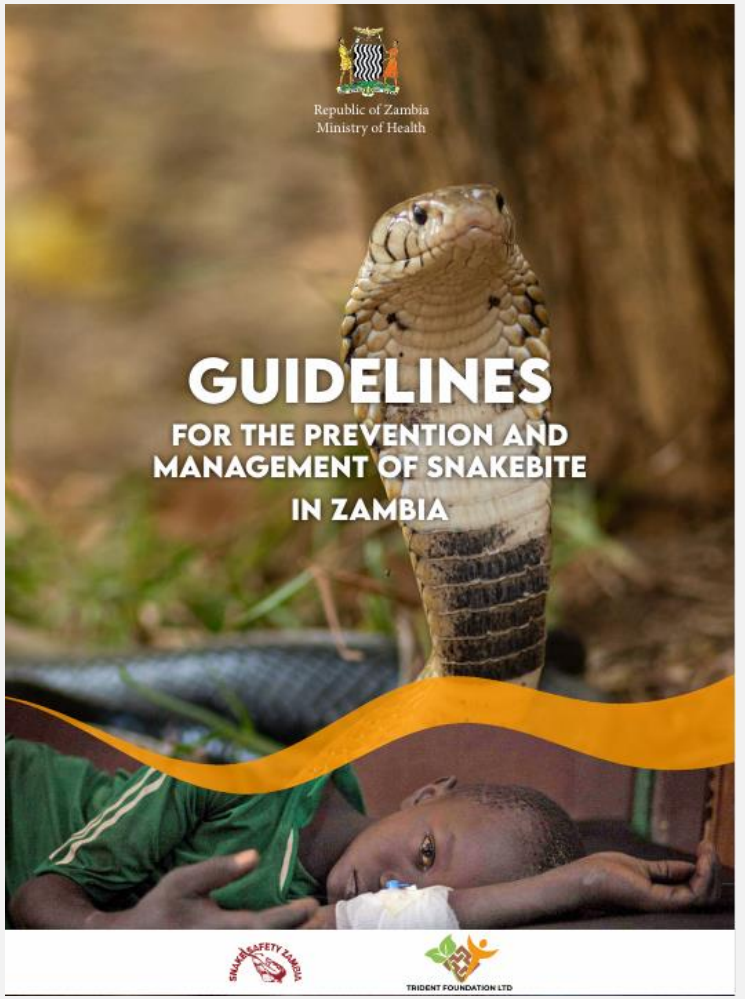


Outputs and Outcomes – African Member States

- Increased international engagement
- Better surveillance and epidemiology
- Better capability from WHO to support MS
- Created or revised national action plans and/or treatment guidelines:

  Eswatini, Kenya, Namibia, South Africa, Zambia
- Consideration for local antivenom manufacturing:

  Cameroon



Acknowledgements

David Williams – Regulation and Prequalification
Bernadette Abela – Neglected Tropical Diseases (NTD)
Anna Pintor – NTD and GIS Centre for Health
Raphael Ruiz de Castaneda - NTD
Bethany Moos - NTD
Kaushi Kanenkege – NTD

multiple colleagues in GIS
a large number of external advisors on several advisory groups!

wellcome for initial funding

World Health Organization


Thankyou
World Health Organization

Monitored emergency use authorization of snake antivenoms

MEURI: Monitored Emergency use of UnRegistered and experimental Interventions

A proven framework

- First proposed in 2014 during Ebola crisis in West Africa
- An adapted model based on the MEURI ethical framework under development to facilitate the emergency use authorisation of new or existing treatments for which clinical data is lacking
- Similar approach to compassionate use authorization schemes for experimental, investigational, or unregistered medicines by Europe's EMA and US FDA

Prerequisites

- Agreement of national government to issue an emergency use authorization and provide national ethics committee oversight
- Robust preclinical data, approved treatment protocol, informed consent, compulsory case reports to independent DSMB for progressive review

Goals

- Facilitate rapid access to existing, new and experimental treatments
- Improve the oversight of antivenoms, particularly in countries where no current provision for clinical trials is required for authorization